REMARKS

This application is a divisional of U.S. Application Serial No. 08/996,422 and is directed to methods of use for the compounds of formula I wherein m=1 and n=1 and pharmaceutical salts thereof. In the parent application restriction was required between the method of using the compounds and the compounds and pharmaceutical compositions. In addition an election of a compound species was required. In the parent application Applicants elected the method of using a species falling within formula I wherein m=1 and n=1, and W-C(H)p C=X is the caprolactam, dibenzo[b,d]azepin-6-one. Accordingly, the claims of the parent application were limited to the method of use of compounds wherein n=1, m=1 and W-C(H)p C=X forms certain defined caprolactams. Applicants reserved the right to file divisional applications to all of the subject matter not examined in the parent application. Therefore, the present amendment cancels all of the original claims and presents new Claims 91-117 directed to the methods of use of the compounds of formula I wherein m=1 and n=1 (defined as formulas IA and IB).

The specification has been amended to provide the cross-reference to the parent application and to correct typographical errors and avoid the use of the same substituent letter having different meanings. Thus where the letters Z and T have been given different meanings in defining a subgenus than given in the generic formula, Z and T have been changed to Z^a and T^a or T^b. Z has been redefined as Z′ in the claims deleting the C(O) group from the definition because it now appears in the generic structural formula and omitting the case where T is -O- or -S- and X′ or X″ is hydrogen or fluoro. Table 7C (page 597) has also been amended to correct an error in the compound formula for 7C-214 in omitting the alaninyl moiety. Since this compound was prepared via a coupling reaction using an alaninyl-starting material, the product obviously must also contain an alaninyl-group. The specification has also been amended to provide antecedent basis for the cyclic formulas recited in original Claims 17, 19, 21 22, 24-27 and 30-31. These amendments have also been made in the parent application. In addition the specification has been

amended to provide antecedent basis for formula IA, recited in new Claims 91-93 representing the subgenus wherein m=1 and n=1 and for formula IB in new Claim 95-97, wherein m=1 and n=1 but grouping the cyclic substituents (Q) recited in original Claims 17, 19, 21, 22 and 24-27.

New Claims 91-112 and 114-116 generally correspond to and are supported by the original method claims defined for the case wherein m=1 and n=1 and excluding the subject matter examined in the parent application. Support for the new method claims of formula IA, i.e. Claims 91-93, can be found in original Claims 1-3 wherein m=1 and n=1. Support for new Claim 94 can be found in original Claim 16. Support for the new method claims of formula IB, Claims 95-97, can be found in original Claims 17-31. In addition, the definition of R^2 in Claims 91-97 has been modified to provide antecedent support for the terms 2-aminopyridyl, 2-methylcyclopentyl, cyclohex-2-enyl and $-(CH_2)_4NHC(O)OC(CH_3)_3$ recited in Claim 114; see original Claim 15 and page 17, lines 8-30 of Applicants' specification. In the substituent group $-(CH_2)_4N$-Boc, the term Boc has been replaced by *t*-butyloxycarbonyl (shown above) in accordance with the definition of Boc set forth on page 214 of the specification. Support for the inclusion of pharmaceutically acceptable salts can be found in the definition on page 160, lines 10-17 and original Claim 90. Claims 98-112 are ultimately dependent upon Claims 95-97 and support can be found in original Claims 17-31. Support for new Claim 113 more particularly defining the substituent group R^1, can be found on page 14, line 28 through page 15, line 23 of the specification. Support for Claim 114 can be found in original Claim 13. In Claim 114, the formula $CH_3C(=NOH)CH_2-$ and the formula for the 1,5-dimethyl-hex-4enyl, correct obvious typographical errors found in original Claim 13 (page 755, line 4 and page 754, line 16 respectively). Further support for the first correction can be found in original Claim 90 and the compound 5-{N'-(4-(hydroxyimino)pentanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one. Support for Claims 115 and 116 more particularly defining the substituent group R^2 can be found in original Claims 14 and 15. Lastly, support for Claim 117 more particularly defining Z' can be

found in the definition of Z for example on page 10, lines 18-21 and in the compounds recited on pages 18-86 of the specification, which exemplify the case where Z' is $-CH_2-$.

Further, unless otherwise defined in the claims, the new claims now expressly recite that the terms aryl, aryloxy, alkaryl, heteroaryl and heterocyclic are optionally substituted to conform with the definitions of these terms in Applicants' specification; i.e. page 156, line 24 - page 157, line 9; page 157, lines 11-12; page 153, lines 27-29; page 158, lines 14-25 and page 158, line 27 - page 159, line 7, respectively.

Examination and allowance are respectfully requested.

In the event the Examiner has any questions concerning the Preliminary Amendment or the Application, the Examiner is requested to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: Lawrence S. Squires
Lawrence S. Squires
Registration No. 24,060

P.O. Box 1404
Alexandria, Virginia 22313-1404
(650) 622-2300

Date: July 26, 2001

Attachment A

Marked up version of the Specification

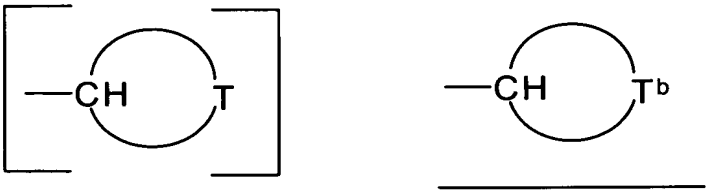
In accordance with the provisions of 35 U.S.C. §1.121(b)(iii), Applicants submit a marked up copy of the amendments made to the specification.

On page 1, paragraph 1 under "Cross reference to Related Applications" replace with the following:

This application [claims the benefit of] is a division of U.S. Application Serial No. 08/996,422 filed December 22, 1997, which claims priority under 35 U.S.C. §119(e) from U.S. Provisional Application No. 60/064,851 which was converted pursuant to 37 C.F.R. §1.53(b)(2)(ii) from U.S. Patent Application No. 08/780,025 filed December 23, 1996.

On page 87 paragraph 1, line 1-21 please replace with the following:

Preferred cyclic groups defined by W and $-C(H)_pC(=X)-$ include cycloalkyl, lactone, lactam, benzazepinone, dibenzazepinone and benzodiazepine groups. In one preferred embodiment, the cyclic group defined by W and $-C(H)_pC(=X)-$, forms a cycloalkyl group of the formula:

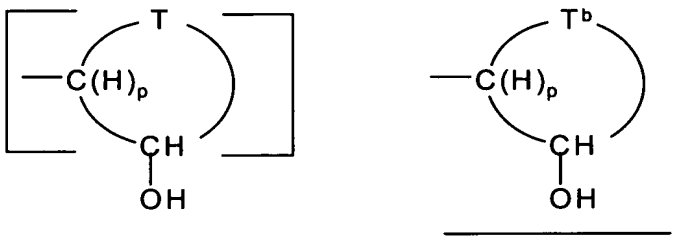


wherein [T] T^b is selected from the group consisting of alkylene and substituted alkylene.

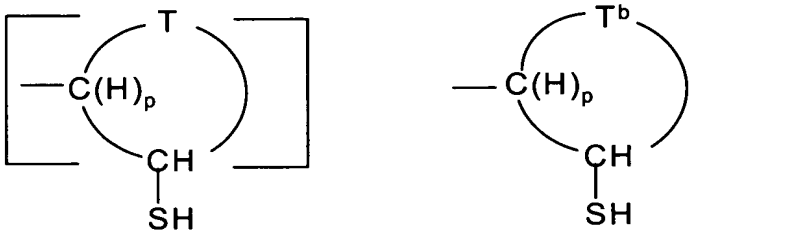
On page 88, second full paragraph starting on line 8 through page 89, line 8 replace with:

In another preferred embodiment, the cyclic group defined by W, together with $-C(H)_pC(=X)-$ is a ring of the formula:

Attachment A



or



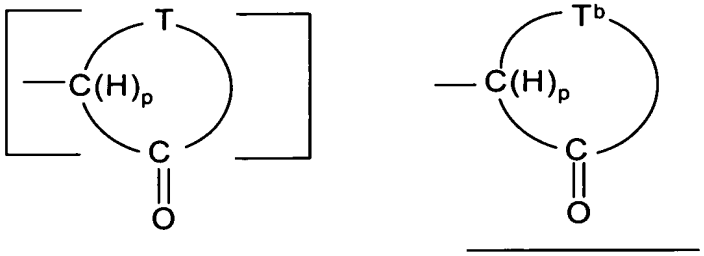
wherein *p* is zero or one, [T] T^b is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $-(R^{21}Z^a)_qR^{21}-$ and $-Z^aR^{21}-$ where Z^a is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] Z^a is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the
-O- or -S-, and *q* is an integer of from 1 to 3.

On page 90, second full paragraph starting at line 9 through page 91, line 10 replace with:

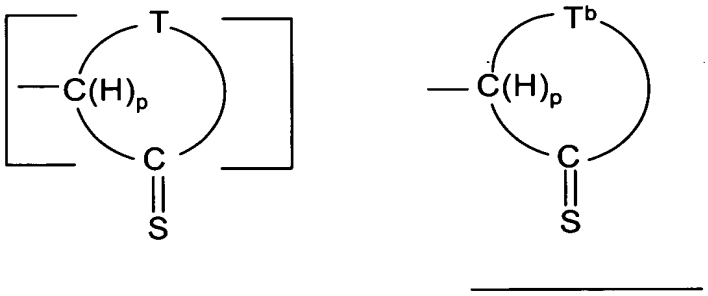
Yet another preferred embodiment of the cyclic group defined by W, together with

Attachment A

$-C(H)_pC(=X)-$, is a ring of the formula:



or



wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the

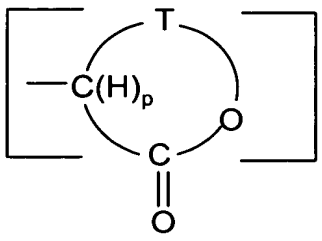
-O- or -S-, and *q* is an integer of from 1 to 3.

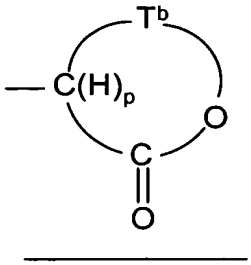
On page 92, second full paragraph starting at line 7 through page 93, line 37, replace with:

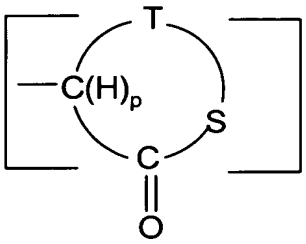
In another preferred embodiment, the cyclic group defined by W, together with

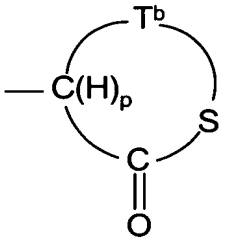
Attachment A

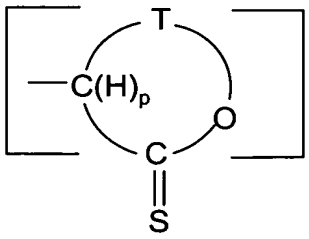
$-C(H)_pC(=X)-$, forms a ring of the formula:

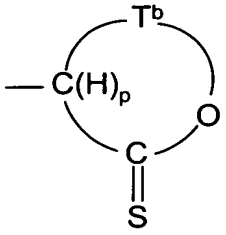






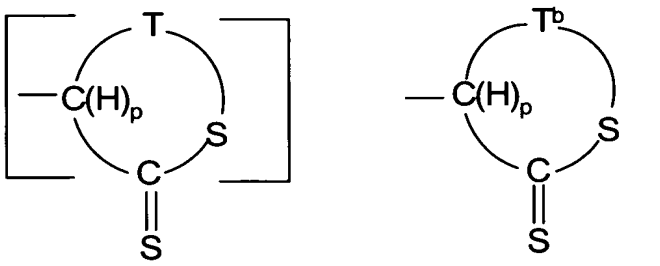






or

Attachment A

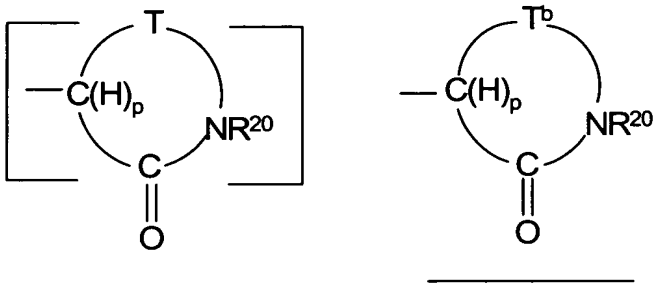


wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the
-O- or -S-, and *q* is an integer of from 1 to 3.

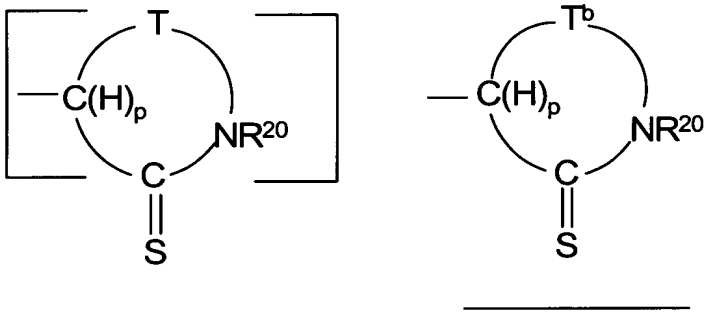
On page 94, second full paragraph, starting on line 20 through page 95, line 30, replace with:

In another preferred embodiment, the cyclic group defined by W and $-C(H)_pC(=X)-$, forms a lactam ring of the formula:

Attachment A



or a thiolactam ring of the formula:



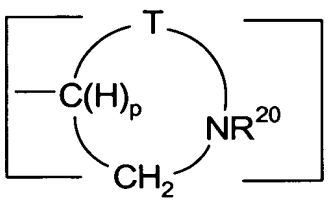
wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the

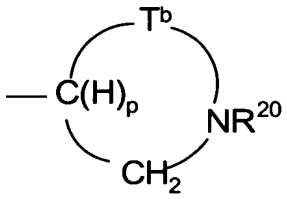
-O- or -S-, and *q* is an integer of from 1 to 3.

Attachment A

On page 99, first paragraph on lines 1-22, replace with:

In another preferred embodiment, the cyclic group defined by W, together with $-C(H)_pC(=X)-$, forms a ring of the formula:



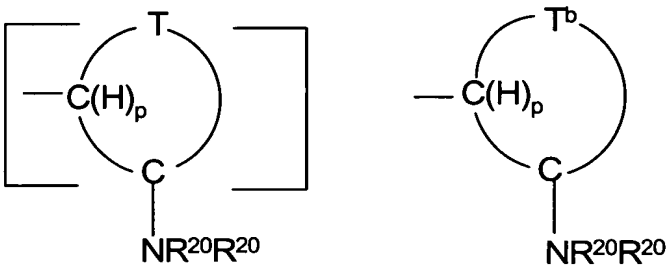


wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the
-O- or -S-, and *q* is an integer of from 1 to 3.

On page 99, second full paragraph starting at line 24 through page 100, line 10, replace with:

A still further preferred embodiment is directed to a ring group defined by W, together with $-C(H)_pC(=X)-$, of the formula:

Attachment A



wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the

-O- or -S-, and *q* is an integer of from 1 to 3.

Attachment A

Please replace page 597 of Table 7C with the section of the table below:

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-214	5{N'-(dl-mandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	dl-mandelic acid or dl-alpha-hydroxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2
7C-215	5-{N'-(p-chloromandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	p-chloromandelic acid (Acros)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2, 478.1
7C-216	5-{N'-(1-alpha-hydroxyisocaproyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	1-alpha-hydroxyisocaproic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	424.2
7C-217	5-{N'-(4-bromomandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-bromomandelic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	522.1, 524.1
7C-218	5-{N'-(1-(+)-lactyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	1-(+)-lactic acid (Sigma)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	382.2, 454.2
7C-219	5-{N'-(d-3-phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	d-3-phenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2